and 2′,3′-cNADP [1], and the neuronal protein p42^{IP4} [2]. We compared the mPTP opening parameters in non-synaptic brain mitochondria from young and old rats. In mitochondria from old rats (>18 months), mPTP opening occurred at a lower threshold calcium concentration than in mitochondria from young rats (<3 months). mPTP opening in mitochondria from old rats was accelerated by 2′,3′-cAMP, which also lowered the threshold calcium concentration. In non-synaptic mitochondria from old rats, the CNP level was decreased by 87%. This was accompanied with decreased levels of voltage-dependent anion channel (VDAC) and of p42^{IP4}. Thus, reduced mitochondrial level of CNP and activity could lead to a rise in the concentration of the mPTP promoter 2′,3′-cAMP. We propose that in aging diminished levels of these proteins lead to mitochondrial dysfunction, in particular, to decreased threshold calcium concentration for mPTP induction. The level of CNP and p42^{IP4} and, probably VDAC, might be essential for myelination and electrical activity of axons. That might be the steps of age-related mitochondrial dysfunction, resulting in myelin and axonal pathology. We demonstrate that the levels of three mitochondrial proteins (CNP, p42^{IP4}, and VDAC) decreased in mitochondria with aging. These three proteins are related to the calcium-transporting system in mitochondria and the regulation of mPTP function. A diminished level of these proteins leads to mitochondrial dysfunction, in particular, increased calcium uptake and decrease of threshold calcium concentration. That causes mPTP induction and might be the initial step of mitochondrial dysfunction, resulting in myelin and axonal pathology.

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doi:10.1016/j.bbabio.2012.06.269

13P9

Mitochondrial dysfunction in MnSOD knockout mice

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Oxidative stress is implicated to be the cause of several pathological conditions in the cell. Therefore mechanisms reducing ROS levels in the cell are carefully investigated. One of the antioxidant enzyme MnSOD, which is located in the mitochondrial matrix, attracts special attention, because mitochondria are suggested to be a major source of ROS production. Introduced in the 90th of the last century, MnSOD knockout mouse is a useful model to investigate the consequences of reduction of antioxidant reactions within mitochondria. This knockout mouse model was generated via inactivation of the MnSOD gene by homologous recombination [1]. Despite of the available data in characterizing the pathological phenotype of MnSOD knockout mouse, conclusive results concerning homozygous mice are still limited, because homozygous mutant mice die during the first days after birth. Therefore, we analyzed the impact of MnSOD knockout on mitochondria from different tissues of newborn mice. Mitochondrial function was investigated in the brain, liver, heart and muscle. The enzyme activities of aconitase, citrate synthase and mitochondrial complexes I and IV were measured in tissue homogenates from wild type, heterozygous and homozygous mice. In accordance with the literature aconitase activity was reduced in all tissues under investigation. A significant reduction of complex I activity was observed in liver homogenates of homozygous mice. Additionally, we analyzed oxygen consumption in tissue homogenates. Interestingly, while complex I activity in brain homogenates was only slightly reduced, respiration rates with complex I supported substrates were significantly decreased in homozygous mouse brain homogenates. Taken together, our findings demonstrate a tissue specific distribution of mitochondrial dysfunction in MnSOD knockout mice.

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doi:10.1016/j.bbabio.2012.06.270

13P10

Oxidation of cardiolipin in liposomes: A new insight into the primary steps of mitochondria-triggered apoptosis

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Cardiolipin is an unusual lipid that is present almost exclusively in the coupling membranes. Cardiolipin is abundant in the inner mitochondrial membrane, being tightly bound within the proteins of respiratory complexes and apparently required for their proper functioning. In addition, cardiolipin represents the major target for reactive oxygen species and its oxidation is regarded as a primary signal of mitochondria-induced apoptosis [1,2]. The present study introduces an approach where the impact of diverse antioxidants on the peroxidation of cardiolipin could be investigated with a liposome model based on the cardiolipin from bovine heart. The data obtained suggest how the changes in the condition of the respiratory chain enzymes can trigger the oxidation of cardiolipin molecules.

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doi:10.1016/j.bbabio.2012.06.271

13P11

Reactive oxygen species production by flavin dehydrogenases of the mitochondrial respiratory chain

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